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10/820,647	04/07/2004	Kevin Liu	063768-0309115	8504

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	**PAPER NUMBER**
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,647	LIU ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *50 and 70* is/are allowed.

6)☒ Claim(s) *1-17,19-36,48,49,51-53,57-61 and 65-69* is/are rejected.

7)☒ Claim(s) *18,37-47,54-56 and 62-64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060420*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-70 are pending in this application.

Election/Restrictions

Applicant's election with traverse of Group I (Claims 1-70 drawn to compounds and methods of formula I wherein Ar_1 is pyrimidine) in the reply filed on November 1, 2006 is acknowledged. The traversal is on the ground(s) that the restriction is improper. This is not found persuasive because the compounds of Groups I-IV are structurally dissimilar and are not art recognized equivalents. They are structurally dissimilar such that a reference anticipating a compound of Group I may not render the compounds of Groups II-IV obvious or vice-versa. 37 CFR 1.141(a) provides that two or more independent and distinct inventions may not be claimed in one application, whether or not the misjoinder occurred in one claim or more than one claim. Restriction is going to be exercised where independent and distinct inventions are presented in one Markush grouping. Independent means when the compound is being made and/or used alone, not in combination with other compounds of the Markush expression. Restriction is considered proper in Markush claims where the members are so diverse and unrelated that a prior art reference anticipating the claim with respect to one of the members, would not render the claims obvious under 35 U.S.C. 103 with respect to the other members. Therefore, what should be considered for patentable distinctness is the compound as a whole. Each of the groups are classified separately and further, the compounds of Groups I-IV require separate searches in the literature and therefore, it is burdensome for the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of the species of the compound of Example 7a is acknowledged. As the elected species was not found in the prior art, the search was expanded to the compounds of the elected invention of Group I.

Claims 1-49 and 51-69 (in part, wherein Ar1 is other than pyrimidine) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 1, 2006.

Claim Objections

Claims 18, 37-47, 54-56 and 62-64 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. Also, a multiple dependent claim may not depend from any other multiple dependent claim. See MPEP § 608.01(n).

Claims 18, 37, 41, 43 and 47 recite "any of claim 4 and claim 5" and therefore, do not refer to the claims in the alternative. These claims should be amended to recite -- any <u>one</u> of claim 4 <u>or</u> claim 5 -- to be in proper form.

Claim 54 refers to claim 53 and claim 3. Claim 62 refers to "any of claims 59-61" and claim 3; claim 63 refers to "any of claims 59-61" and claim 4; and claim 64 refers to "any of claims 59-61" and claim 5. These multiply dependent claims do not refer to the claims in the alternative.

Claim 55 multiply depends from claim 54 and claim 3 of which claim 54 is a multiple dependent claim. A multiple dependent claim may not refer to any other multiple dependent claim.

Accordingly, the claims 18, 37-47, 54-56 and 62-64 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-17, 19-36, 48-49, 51-53, 58-61 and 66-69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound of Formula I or a pharmaceutically acceptable N-oxide or salt thereof, does not reasonably provide enablement for a pharmaceutically acceptable **prodrug, metabolite, ester, amide** or **solvate** thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The instant claim recites "A compound ... or a .... pharmaceutically acceptable prodrug, pharmaceutically active metabolite, ... pharmaceutically acceptable ester, pharmaceutically acceptable amide, or pharmaceutically acceptable solvate thereof" wherein there is insufficient description in the specification regarding the types of 'prodrugs, metabolites, esters, amides and solvates' intended by the recitation. The specification at page 27 provides a definition for the term "prodrug", however, does not provide any explanation of the terms 'pharmaceutically active metabolite or pharmaceutically acceptable solvate' of the compounds of Formula I. The term 'prodrug' generally known to represent 'a physiologically functional derivative, for example, an ester or an amide, which upon administration to a mammal is capable of providing (directly or indirectly) a compound of the invention or an active metabolite thereof'. In the instant case, however, the specification does not provide what are some of the examples of "derivatives" intended by the terms 'prodrugs, metabolites, esters, amides' etc..

The term 'prodrug' and/or 'metabolite' is directed to esters and amides of compounds of Formula I. However, the definition of various substituent groups in Formula I already include such groups, i.e., acids, esters, amides, etc. The specification does not provide what other 'compounds' of the invention are intended to be the above referred "prodrugs" and "metabolites". The generic formula of the claims already include both esters and the corresponding free acid forms, see e.g., see the term " $-C(O)OR_4$", wherein R_4 is independently H, alkyl, etc. There is no disclosure regarding any other esters or amides that are capable of providing compounds of the invention. Further, specification does not provide sufficient explanation of the term "metabolite". A metabolite is any compound which is pharmaceutically active *in vivo* when it undergoes "metabolic" process and the specification does not provide any

disclosure of what these compounds might be that *in vivo* transform in to the instantly claimed compounds. The specification does not provide what other 'compounds' of the invention are intended to be metabolites. Since functional groups such as esters, amides, etc. are already included in the claimed compounds, it is not clear whether compounds bearing these groups are excluded from being a potential "pharmaceutically acceptable **prodrug, metabolite, ester, amide** or **solvate**" of the claimed invention. If compounds bearing these groups (i.e., ester, etc.), which are likely to undergo *in vivo* transformation, are excluded then what is included in the definition of the above term and where on the structural Formula I are these groups placed; the specification does not provide any direction to one of ordinary skill in the art.

A prodrug as defined by Bundgaard (Design of Prodrugs) "is an inactive species, and therefore, once its job is completed, intact prodrug represents unavailable drug" (see page 1). Thus, an important requirement of prodrugs is that they be pharmacologically inactive. The scope of the term 'prodrugs' is quite broad. A state of the art reference, Silverman (The Organic Chemistry of Drug Design and Drug Action) teaches many strategies for making prodrugs. Among them are polymer-bound prodrugs (pages 369-374), acyclic prodrugs which form heterocyclic compounds *in vivo* (page 360), conjugates consisting of two or more drug molecules which are cleaved into active drug molecules (page 377), amine precursors which are converted to amines *in vivo* (page 358), and drugs bound to a carrier via a linker (page 374). Applicant has neither described nor provided working examples for the combination of the invention compound with various types of 'other compounds' or 'pharmaceutical excipients' intended by the instant claim language. In a clinical trial setting, it would require undue experimentation to determine whether a particular compound meets the criteria of a 'prodrug'.

Further, the specification has no working examples of "solvate" of compound of Formula I; and some of the exemplified compounds within the claimed genus were in contact with solvent. Yet they have not formed solvate as evident form spectral data provided for these compounds.

Searching the pertinent art in the related pyrimidine area did not result in support for such solvates of instant pyrimidine compounds. Searching the more general area of solvates resulted in pertinent reference West applied below. West clearly shows lack of predictability of the art in the solvate area.

Based on these two facts, a scope of enablement rejection follows using relevant Wands factors. Hence, the burden of establishing the *prime facie* case is met with.

(i). **The nature of the invention and the state of the prior art:**

Specification is not adequately enabled as to how to make solvate of compounds of Formula I Specification has no example of solvate of the instant compounds. Specification neither defines the term nor provides an enabling disclosure of 'solvates' of the instant compounds.

The compound of Formula I embrace substituted pyrimidine compounds substituted with variable groups R_1, R_3, etc.

Careful calculation of the number of compounds embraced in the instant Formula I shows a large number of compounds and there is no teaching of any solvate of this large genus.

Search in the pertinent art, including water as solvent resulted in a pertinent reference, which is indicative of unpredictability of solvate formation in general. The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language

of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate. In the instant case of solvate a similar reasoning therefore apply. Water is a solvent and hence it is held that a pertinent detail of West, which relates to solvates, is also applicable to water.

In addition, an additional search resulted in Vippagunta et al., Advanced Drug Delivery Reviews 48: 3-26, 2001, which clearly states that formation of solvates in unpredictable. See entire document especially page 18, right column section 3.4. Note Vippagunta et al., states "Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for series of related compounds".

Joachim Ulrich (Kirk-Othmer Encyclopedia of Chemical Technology) provides that "Pseudopolymorphs are solvates or in the case of water as solvent, hydrates, which means crystals that incorporate solvent molecules into the crystal lattice. Pseudopolymorphs exhibit different crystal forms and/or different densities, solubilities, dissolution rates, colors, hardnesses, etc. Compared with polymorphs, there is an additional degree of freedom (than

temperature and pressure), which means a different solvent or even the moisture of the air that might change the stabile region of the pseudopolymorph".

(ii). **The predictability or lack thereof in the art:**

Hence the solvate as applied to the above-mentioned compounds claimed by the applicant are not art-recognized compounds and hence there should be adequate enabling disclosure in the specification with working example(s).

(iii). **The amount of direction or guidance present:**

Examples illustrated in the experimental section are limited to making the compounds not related to solvates. There is no example of solvate of instant compound. Many of the exemplified compounds were shown in the specification that have come in contact with water and/or other solvent but there is showing that these compounds formed solvates. Hence it is clear that merely bringing the compound and water or solvent together does not result in solvate and additional direction or guidance is needed to make them - specification has no such direction or guidance.

(iv). **The presence or absence of working examples:**

There is no working example of any solvate formed. The claims are drawn to solvate, yet the numerous examples presented all failed to produce a solvate or even solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "[T]he specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such compounds exist... the examples of the patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance

appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, there should be showing supporting that solvates of these compounds exists and therefore can be made.

(v). **The breadth of the claims & the quantity of experimentation needed:**

Specification provides no support, as noted above, for compounds generically embraced in the claim 1 would lead to desired solvate of the compound of Formula (I). As noted above, the genus embraces a large number of compounds and hence the claims are extremely broad. The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired **solvate** of compound of Formula I embraced in the instant claims in view of the pertinent reference teachings.

2. Claims 51-53, 57-61 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treatment of diabetes, does not reasonably provide enablement for a method of modulating a peroxisome proliferators-activated receptor (PPAR) function; a method of inhibiting the formation of adipocytes in a mammal; a method of treating a disease generally; a method of treating a PPAR-modulated disease or condition or a metabolic disorder generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification fails to enable one skilled in the art to use the claimed compounds. The use disclosed in the specification is as PPAR regulators, useful as hypoglycemic agents, etc., see page 1. Test assays to measure PPAR binding activity are provided at pages 21-22, however, no results are provided for any of the exemplified compounds. The data provided in the specification is insufficient such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the instantly claimed compounds. This area of receptor activity is highly structure specific and unpredictable as can be seen from the range of the results obtained for the tested compounds. Further, there is no evidence on record which demonstrates that the *in-vitro* screening tests relied upon are recognized in the art as being reasonably predictive of success in any of the contemplated areas of regulating PPAR. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study"). Fayer et al. (PubMed abstract) report that such correlation or lack thereof is important to predict drug-drug interactions. This clearly highlights the unpredictability in the art and the need for undue experimentation. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds as PPAR regulators.

The instant claims 51-52 recite "a method of modulating a PPAR function" wherein the term "modulating" generally encompasses blocking, activating, partial blocking and partial

activating. However, the compounds were not shown to have all these properties. For example, it is revolutionary for a compound to be effective as a blocker, activator and partial blocker/activator. The specification did not provide any competent tests or data to establish that the compounds have the claimed 'calcium sensing receptor modulating activity'. The remaining claims recite 'a method of inhibiting the formation of adipocytes'' 'a method of treating a disease is comprising identifying a patient in need thereof'; etc. The instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through to the corresponding therapeutic method of any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

Claims are drawn to a method for treatment of 'a PPAR-modulated disease or condition' and the specification provides a select list of disorders such as diabetes, hyperinsulinemia, atherosclerosis, etc. However, the instant claim includes disorders that are known to exist and those that may be discovered in the future and therefore, is extremely broad. For example, atherosclerosis is a common form of arteriosclerosis associated with the formation of atheromas which are deposits of yellow plaques containing cholesterol, lipids, and lipophages within the intima and inner media of arteries. This results in a narrowing of the arteries, which reduces the blood and oxygen flow to the heart and brain as well as to other parts of the body and can lead to a heart attack, stroke, or loss of function or gangrene of other tissues.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed methods.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17, 19-36, 48-49, 51-53, 58-61 and 66-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. Claim 1 recites: "A compound having the structure of Formula I: .... or .... ester, ... amide, ... thereof", wherein the use of the terms "ester", "amide" is deemed as indefinite. The definition of various substituent groups in the formula already includes free acids as well as esters, amides (see e.g., the definition of B, which includes – $C(O)OR_4$ wherein R_4 is H, alkyl, etc.). Therefore, it is not clear what is the difference between the substituent groups already recited and the 'ester', which is specifically recited in the claims. Since the functional groups such as esters, amides, etc. of the compounds of Formula I are already included in the claim, deletion of the terms 'pharmaceutically acceptable ester' and 'pharmaceutically acceptable amide' from the claims is suggested.

2. In claim 21, the recitation "... **any of** claim 20" is not proper claim language. Deletion of the term 'any of' is suggested.
3. Claim 51 recites the steps: "and monitoring a change in cell type, cell proliferation, activity of said PPAR, or binding of said PPAR with a natural binding partner" without providing any explanation what is intended by these steps. The specification does not provide any help.
4. Claim 58 recites "A method of treating a disease comprising identifying a patient in need thereof" – without actually specifically providing 'which disease' is intended. The specification does not provide any help.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 14-17, 19-29, 32-36, 51-53, 58-61 and 66 are rejected under 35 U.S.C. 102(e) as being anticipated by Cantin et al., WO 04/058174 (effective filing date December 20, 2002). The instant claims read on reference disclosed compounds, see the compound of structural formula (I) in page 2 and the corresponding species of Examples 282-289, 292-300, etc. The

compounds are disclosed to be useful as pharmaceutical agents for the treatment of diabetes, obesity, etc., see page 198, starting at paragraph [584].

Note: Applicant's claim for domestic priority under 35 U.S.C. 119(e) based on application No. 60/464,581 filed April 17, 2003 is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for the claims of this application. Particularly, the provisional applications does not fully support the recitations in the claims: "a pharmaceutically active metabolite"; "a pharmaceutically acceptable solvate", etc. Further, the prior application recites that "Ar_1 is a five-membered or six-membered heteroaryl ring" as compared to the definition of Ar_1 in the instant claim – "selected from a monocyclic heteroaromatic ring structure and a bicyclic heteroaromatic ring structure". Further, in the prior application, B is defined as $-CH_2$-C(O)OR_4 as compared to the instant claims wherein B is $-(CH_2)_j$-C(O)OR_4. (The above is a representative list of the differences between the instant claims and the priority document and is not a complete list of all of the differences between the claims and the priority document).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 14-17, 19-29, 32-36, 51-53, 58-61 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantin et al., WO 04/058174. The reference teaches a generic group of pyrimidine compounds, which embraces applicant's instantly claimed compounds. See formula (I) in page 2, and the species of Examples 282-289, 292-300, etc. The compounds are taught to be useful as pharmaceutical agents for the treatment of diabetes, obesity, etc., see page 198, starting at paragraph [584]. The instant claims differ from the reference by reciting specific species or a more limited subgenus than the reference. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ

423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Allowable Subject Matter

Claims 50 and 70 are allowed. The references of record do not teach or fairly suggest the instantly claimed compound.

Receipt is acknowledged of the Information Disclosure Statement filed on April 20, 2006 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

January 7, 2007